

SEQUENCE LISTING

<110> Shenoy, Sudha
Lefkowitz, Robert J.

<120> Modified Trafficking Patterns for Arrestin and G-Protein-Coupled Receptors via Arrestin-Ubiquitin Chimera

<130> 186563/US/2 (469390-00352)

<140> US 10/543,122

<141> 2004-01-26

<150> US 60/442,403

<151> 2003-01-24

<160> 45

<170> PatentIn version 3.3

<210> 1

<211> 1581

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Leu Tyr Lys Ser Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala	
20 25 30	
gtc gac ggt acc acg cgc acc atg ggt gaa aaa ccc ggg acc agg gtc	144
Val Asp Gly Thr Thr Arg Thr Met Gly Glu Lys Pro Gly Thr Arg Val	
35 40 45	
ttc aag aag tcg agc cct aac tgc aag ctc acc gtg tac ttg ggc aag	192
Phe Lys Lys Ser Ser Pro Asn Cys Lys Leu Thr Val Tyr Leu Gly Lys	
50 55 60	
cgt gac ttt gtg gat cac ttg gac aaa gtg gat cct gtc gat ggt gtg	240
Arg Asp Phe Val Asp His Leu Asp Lys Val Asp Pro Val Asp Gly Val	
65 70 75 80	
gtg ctt gtg gat cct gac tac ttg aag gac cgg aaa gtg ttt gtg acc	288
Val Leu Val Asp Pro Asp Tyr Leu Lys Asp Arg Lys Val Phe Val Thr	
85 90 95	
ctc acc tgt gcc ttc cgc tat ggc cga gaa gac ctg gat gta ctg ggc	336
Leu Thr Cys Ala Phe Arg Tyr Gly Arg Glu Asp Leu Asp Val Leu Gly	
100 105 110	
ctg tct ttc cgc aaa gat ctg ttc atc gcc acc tac cag gcc ttc ccc	384
Leu Ser Phe Arg Lys Asp Leu Phe Ile Ala Thr Tyr Gln Ala Phe Pro	

115	120	125	
ccc atg ccc aac cca cct cgg ccc ccc acc cgc cta cag gac cga ctg Pro Met Pro Asn Pro Pro Arg Pro Pro Thr Arg Leu Gln Asp Arg Leu 130 135 140			432
ctg aag aag ttg ggc cag cat gcc cac ccc ttt ttt ttc aca ata ccc Leu Lys Lys Leu Gly Gln His Ala His Pro Phe Phe Phe Thr Ile Pro 145 150 155 160			480
cag aat ttg cct tgc tcc gtc aca ctg cag cca gga ccg gag gac aca Gln Asn Leu Pro Cys Ser Val Thr Leu Gln Pro Gly Pro Glu Asp Thr 165 170 175			528
ggg aag gcc tgt gga gta gac ttt gag att cga gcc ttc tgt gcc aaa Gly Lys Ala Cys Gly Val Asp Phe Glu Ile Arg Ala Phe Cys Ala Lys 180 185 190			576
tct ata gaa gaa aaa agc cac aaa agg aac tcc gtg cgg ctt atc atc Ser Ile Glu Glu Lys Ser His Lys Arg Asn Ser Val Arg Leu Ile Ile 195 200 205			624
aga aag gta cag ttt gct cct gag aca ccc ggc ccc cag cca tca gct Arg Lys Val Gln Phe Ala Pro Glu Thr Pro Gly Pro Gln Pro Ser Ala 210 215 220			672
gaa acc aca cgc cac ttc ctc atg tct gac cgg agg tcc ctg cac cta Glu Thr Thr Arg His Phe Leu Met Ser Asp Arg Arg Ser Leu His Leu 225 230 235 240			720
gag gct tcc ctg gac aaa gag ctg tac tac cat ggg gaa ccc ctc aat Glu Ala Ser Leu Asp Lys Glu Leu Tyr Tyr His Gly Glu Pro Leu Asn 245 250 255			768
gtc aac gtc cac gtc acc aac aat tct gcc aag acc gtc aag aag atc Val Asn Val His Val Thr Asn Asn Ser Ala Lys Thr Val Lys Lys Ile 260 265 270			816
aga gtg tct gtg aga cag tat gcc gac att tgc ctc ttc agc acc gcg Arg Val Ser Val Arg Gln Tyr Ala Asp Ile Cys Leu Phe Ser Thr Ala 275 280 285			864
cag tac aag tgt cct gtg gct cag ctt gaa caa gat gac cag gtg tct Gln Tyr Lys Cys Pro Val Ala Gln Leu Glu Gln Asp Asp Gln Val Ser 290 295 300			912
ccc agt tcc aca ttc tgc aag gtg tac acc ata acc ccg ctg ctc agt Pro Ser Ser Thr Phe Cys Lys Val Tyr Thr Ile Thr Pro Leu Leu Ser 305 310 315 320			960
gac aac cca gag aag cgt ggc ctt gcc ctt gat ggg caa ctc aag cac Asp Asn Pro Glu Lys Arg Gly Leu Ala Leu Asp Gly Gln Leu Lys His 325 330 335			1008
caa gac acc aac ctg gct tcc agc acc att gtg aag gag gga gcc aac Gln Asp Thr Asn Leu Ala Ser Ser Thr Ile Val Lys Glu Gly Ala Asn 340 345 350			1056
aag gag gtg ctg gga atc cta gta tcc tac agg gtc aac gtg aag ctg Lys Glu Val Leu Gly Ile Leu Val Ser Tyr Arg Val Asn Val Lys Leu 355 360 365			1104
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gcc ccc cgg gaa ata gac atc cct gtg gat acc aac ctc att gaa ttc Ala Pro Arg Glu Ile Asp Ile Pro Val Asp Thr Asn Leu Ile Glu Phe 405 410 415			1248
gat acc aac tat gcc aca gac gac gac atc gtg ttt gag gac ttt gcg Asp Thr Asn Tyr Ala Thr Asp Asp Asp Ile Val Phe Glu Asp Phe Ala 420 425 430			1296
agg ctt cgg ctg aag ggg atg aag gat gac gac tgt gat gac cag ttc Arg Leu Arg Leu Lys Gly Met Lys Asp Asp Asp Cys Asp Asp Gln Phe 435 440 445			1344
tgc gtc gac cag atc ttc gtg aag act ctg act ggt aag acc atc acc Cys Val Asp Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr 450 455 460			1392
ctc gag gtg gag ccc agt gac acc atc gag aat gtc aag gca aag atc Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile 465 470 475 480			1440
caa gat aag gaa ggc att cct cct gat cag cag agg ttg atc ttt gcc Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala 485 490 495			1488
gga aaa cag ctg gaa gat ggt cgt acc ctg tct gac tac aac atc cag Gly Lys Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln 500 505 510			1536
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35 40 45

Phe Lys Lys Ser Ser Pro Asn Cys Lys Leu Thr Val Tyr Leu Gly Lys
50 55 60

Arg Asp Phe Val Asp His Leu Asp Lys Val Asp Pro Val Asp Gly Val
 65 70 75 80
 Val Leu Val Asp Pro Asp Tyr Leu Lys Asp Arg Lys Val Phe Val Thr
 85 90 95
 Leu Thr Cys Ala Phe Arg Tyr Gly Arg Glu Asp Leu Asp Val Leu Gly
 100 105 110
 Leu Ser Phe Arg Lys Asp Leu Phe Ile Ala Thr Tyr Gln Ala Phe Pro
 115 120 125
 Pro Met Pro Asn Pro Pro Arg Pro Pro Thr Arg Leu Gln Asp Arg Leu
 130 135 140
 Leu Lys Lys Leu Gly Gln His Ala His Pro Phe Phe Phe Thr Ile Pro
 145 150 155 160
 Gln Asn Leu Pro Cys Ser Val Thr Leu Gln Pro Gly Pro Glu Asp Thr
 165 170 175
 Gly Lys Ala Cys Gly Val Asp Phe Glu Ile Arg Ala Phe Cys Ala Lys
 180 185 190
 Ser Ile Glu Glu Lys Ser His Lys Arg Asn Ser Val Arg Leu Ile Ile
 195 200 205
 Arg Lys Val Gln Phe Ala Pro Glu Thr Pro Gly Pro Gln Pro Ser Ala
 210 215 220
 Glu Thr Thr Arg His Phe Leu Met Ser Asp Arg Arg Ser Leu His Leu
 225 230 235 240
 Glu Ala Ser Leu Asp Lys Glu Leu Tyr Tyr His Gly Glu Pro Leu Asn
 245 250 255
 Val Asn Val His Val Thr Asn Asn Ser Ala Lys Thr Val Lys Lys Ile
 260 265 270
 Arg Val Ser Val Arg Gln Tyr Ala Asp Ile Cys Leu Phe Ser Thr Ala
 275 280 285
 Gln Tyr Lys Cys Pro Val Ala Gln Leu Glu Gln Asp Asp Gln Val Ser
 290 295 300
 Pro Ser Ser Thr Phe Cys Lys Val Tyr Thr Ile Thr Pro Leu Leu Ser
 305 310 315 320

Asp Asn Pro Glu Lys Arg Gly Leu Ala Leu Asp Gly Gln Leu Lys His
 325 330 335
 Gln Asp Thr Asn Leu Ala Ser Ser Thr Ile Val Lys Glu Gly Ala Asn
 340 345 350
 Lys Glu Val Leu Gly Ile Leu Val Ser Tyr Arg Val Asn Val Lys Leu
 355 360 365
 Val Val Ser Pro Gly Gly Asp Val Ser Val Glu Leu Pro Phe Val Leu
 370 375 380
 Met His Pro Lys Pro His Asp His Ile Thr Leu Pro Arg Pro Gln Ser
 385 390 395 400
 Ala Pro Arg Glu Ile Asp Ile Pro Val Asp Thr Asn Leu Ile Glu Phe
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 Asp Thr Asn Tyr Ala Thr Asp Asp Asp Ile Val Phe Glu Asp Phe Ala
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 Arg Leu Arg Leu Lys Gly Met Lys Asp Asp Asp Cys Asp Asp Gln Phe
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 Cys Val Asp Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
 450 455 460
 Leu Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile
 465 470 475 480
 Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
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gtc Val	gac Asp	ggg Gly 35	acc Thr	acg Thr	cgc Arg	acc Thr	atg Met 40	ggg Gly	gaa Glu	aaa Lys	ccc Pro	ggg Gly 45	acc Thr	agg Arg	gtc Val	144
ttc Phe	aag Lys 50	aag Lys	tcg Ser	agc Ser	cct Pro	aac Asn 55	tgc Cys	aag Lys	ctc Leu	acc Thr	gtg Val 60	tac Tyr	ttg Leu	ggc Gly	aag Lys	192
cgt Arg 65	gac Asp	ttt Phe	gtg Val	gat Asp	cac His 70	ttg Leu	gac Asp	aaa Lys	gtg Val 75	gat Asp	cct Pro	gtc Val	gat Asp	ggg Gly	gtg Val 80	240
gtg Val	ctt Leu	gtg Val	gat Asp	cct Pro 85	gac Asp	tac Tyr	ttg Leu	aag Lys	gac Asp 90	cgg Arg	aaa Lys	gtg Val	ttt Phe	gtg Val 95	acc Thr	288
ctc Leu	acc Thr	tgt Cys	gcc Ala 100	ttc Phe	cgc Arg	tat Tyr	ggc Gly	cga Arg 105	gaa Glu	gac Asp	ctg Leu	gat Asp	gta Val 110	ctg Leu	ggc Gly	336
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ccc Pro 130	atg Met	ccc Pro	aac Asn	cca Pro	cct Pro	cgg Arg 135	ccc Pro	ccc Pro	acc Thr	cgc Arg	cta Leu 140	cag Gln	gac Asp	cga Arg	ctg Leu	432
ctg Leu 145	aag Lys	aag Lys	ttg Leu	ggc Gly	cag Gln 150	cat His	gcc Ala	cac His	ccc Pro	ttt Phe 155	ttt Phe	ttc Phe	aca Thr	ata Ile	ccc Pro 160	480
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ggg Gly	aag Lys	gcc Ala	tgt Cys 180	gga Gly	gta Val	gac Asp	ttt Phe	gag Glu 185	att Ile	cga Arg	gcc Ala	ttc Phe	tgt Cys 190	gcc Ala	aaa Lys	576
tct Ser	ata Ile 195	gaa Glu	gaa Glu	aaa Lys	agc Ser	cac His	aaa Lys 200	agg Arg	aac Asn	tcc Ser	gtg Val	cgg Arg 205	ctt Leu	atc Ile	atc Ile	624
aga Arg 210	aag Lys	gta Val	cag Gln	ttt Phe	gct Ala 215	cct Pro	gag Glu	aca Thr	ccc Pro	ggc Gly	ccc Pro 220	cag Gln	cca Pro	tca Ser	gct Ala	672
gaa Glu 225	acc Thr	aca Thr	cgc Arg	cac His	ttc Phe 230	ctc Leu	atg Met	tct Ser	gac Asp	cgg Arg 235	agg Arg	tcc Ser	ctg Leu	cac His	cta Leu 240	720
gag gct	tcc	ctg	gac	aaa	gag	ctg	tac	tac	cat	ggg	gaa	ccc	ctc	aat		768

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Val	Asn	Val	His 260	Val	Thr	Asn	Asn 265	Ser	Ala	Lys	Thr	Val	Lys 270	Lys	Ile		
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Arg	Val	Ser 275	Val	Arg	Gln	Tyr	Ala 280	Asp	Ile	Cys	Leu	Phe 285	Ser	Thr	Ala		
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Gln	Tyr 290	Lys	Cys	Pro	Val	Ala 295	Gln	Leu	Glu	Gln	Asp 300	Asp	Gln	Val	Ser		
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Pro	Ser	Ser	Thr	Phe	Cys 310	Lys	Val	Tyr	Thr	Ile 315	Thr	Pro	Leu	Leu	Ser 320		
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Asn	Glu	Val 355	Leu	Gly	Ile	Leu	Val 360	Ser	Tyr	Ser	Val	Lys 365	Leu	Lys	Leu		
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Ala	Pro	Arg	Glu	Ile 405	Asp	Ile	Pro	Val	Asp 410	Thr	Asn	Leu	Ile	Glu 415	Phe		
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Asp	Thr	Asn	Tyr 420	Ala	Thr	Asp	Asp	Asp 425	Ile	Val	Phe	Glu	Asp 430	Phe	Ala		
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Cys	Val 450	Asp	Gln	Ile	Phe	Val 455	Lys	Thr	Leu	Thr	Gly 460	Lys	Thr	Ile	Thr		
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caa	gac	aag	gaa	ggt	atc	cct	cca	gat	caa	caa	aga	ttg	atc	ttt	gcc	1488	
Gln	Asp	Lys	Glu	Gly 485	Ile	Pro	Pro	Asp	Gln 490	Gln	Arg	Leu	Ile	Phe 495	Ala		
ggt	agg	cag	cta	gaa	gac	ggt	aga	acg	ctg	tct	gat	tac	aac	att	cag	1536	

Gly Arg Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln
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35 40 45

Phe Lys Lys Ser Ser Pro Asn Cys Lys Leu Thr Val Tyr Leu Gly Lys
50 55 60

Arg Asp Phe Val Asp His Leu Asp Lys Val Asp Pro Val Asp Gly Val
65 70 75 80

Val Leu Val Asp Pro Asp Tyr Leu Lys Asp Arg Lys Val Phe Val Thr
85 90 95

Leu Thr Cys Ala Phe Arg Tyr Gly Arg Glu Asp Leu Asp Val Leu Gly
100 105 110

Leu Ser Phe Arg Lys Asp Leu Phe Ile Ala Thr Tyr Gln Ala Phe Pro
115 120 125

Pro Met Pro Asn Pro Pro Arg Pro Pro Thr Arg Leu Gln Asp Arg Leu
130 135 140

Leu Lys Lys Leu Gly Gln His Ala His Pro Phe Phe Phe Thr Ile Pro
145 150 155 160

Gln Asn Leu Pro Cys Ser Val Thr Leu Gln Pro Ala Pro Glu Asp Thr
165 170 175

Gly Lys Ala Cys Gly Val Asp Phe Glu Ile Arg Ala Phe Cys Ala Lys
180 185 190

Ser Ile Glu Glu Lys Ser His Lys Arg Asn Ser Val Arg Leu Ile Ile
 195 200 205
 Arg Lys Val Gln Phe Ala Pro Glu Thr Pro Gly Pro Gln Pro Ser Ala
 210 215 220
 Glu Thr Thr Arg His Phe Leu Met Ser Asp Arg Arg Ser Leu His Leu
 225 230 235 240
 Glu Ala Ser Leu Asp Lys Glu Leu Tyr Tyr His Gly Glu Pro Leu Asn
 245 250 255
 Val Asn Val His Val Thr Asn Asn Ser Ala Lys Thr Val Lys Lys Ile
 260 265 270
 Arg Val Ser Val Arg Gln Tyr Ala Asp Ile Cys Leu Phe Ser Thr Ala
 275 280 285
 Gln Tyr Lys Cys Pro Val Ala Gln Leu Glu Gln Asp Asp Gln Val Ser
 290 295 300
 Pro Ser Ser Thr Phe Cys Lys Val Tyr Thr Ile Thr Pro Leu Leu Ser
 305 310 315 320
 Asp Asn Arg Glu Lys Arg Gly Leu Ala Leu Asp Gly Gln Leu Lys His
 325 330 335
 Glu Asp Thr Asn Leu Ala Ser Ser Thr Ile Val Lys Glu Gly Pro Asn
 340 345 350
 Asn Glu Val Leu Gly Ile Leu Val Ser Tyr Ser Val Lys Leu Lys Leu
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 Val Val Ser Arg Arg Gly Asp Val Ser Val Glu Leu Pro Phe Leu Leu
 370 375 380
 Met His Pro Lys Pro His His His Ile Thr Leu Pro Arg Pro Gln Ser
 385 390 395 400
 Ala Pro Arg Glu Ile Asp Ile Pro Val Asp Thr Asn Leu Ile Glu Phe
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 Asp Thr Asn Tyr Ala Thr Asp Asp Asp Ile Val Phe Glu Asp Phe Ala
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 Arg Leu Arg Leu Lys Gly Met Lys Asp Asp Asp Ser Asp Asp Gln Phe
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Cys Val Asp Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr
450 455 460

Leu Glu Val Glu Ser Ser Asp Thr Ile Asp Asn Val Lys Ser Lys Ile
465 470 475 480

Gln Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala
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Leu Tyr Lys Ser Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala	
20 25 30	
gtc gac ggt acc acg cgc acc atg ggt gaa aaa ccc ggg acc agg gtc	144
Val Asp Gly Thr Thr Arg Thr Met Gly Glu Lys Pro Gly Thr Arg Val	
35 40 45	
ttc aag aag tcg agc cct aac tgc aag ctc acc gtg tac ttg ggc aag	192
Phe Lys Lys Ser Ser Pro Asn Cys Lys Leu Thr Val Tyr Leu Gly Lys	
50 55 60	
cgt gac ttt gtg gat cac ttg gac aaa gtg gat cct gtc gat ggt gtg	240
Arg Asp Phe Val Asp His Leu Asp Lys Val Asp Pro Val Asp Gly Val	
65 70 75 80	
gtg ctt gtg gat cct gac tac ttg aag gac cgg aaa gtg ttt gtg acc	288
Val Leu Val Asp Pro Asp Tyr Leu Lys Asp Arg Lys Val Phe Val Thr	
85 90 95	
ctc acc tgt gcc ttc cgc tat ggc cga gaa gac ctg gat gta ctg ggc	336
Leu Thr Cys Ala Phe Arg Tyr Gly Arg Glu Asp Leu Asp Val Leu Gly	
100 105 110	

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ccc Pro	atg Met 130	ccc Pro	aac Asn	cca Pro	cct Pro	cgg Arg 135	ccc Pro	ccc Pro	acc Thr	cgc Arg	cta Leu 140	cag Gln	gac Asp	cga Arg	ctg Leu	432
ctg Leu 145	aag Lys	aag Lys	ttg Leu	ggc Gly	cag Gln 150	cat His	gcc Ala	cac His	ccc Pro	ttt Phe 155	ttt Phe	ttc Phe	aca Thr	ata Ile	ccc Pro 160	480
cag Gln	aat Asn	ttg Leu	cct Pro	tgc Cys 165	tcc Ser	gtc Val	aca Thr	ctg Leu	cag Gln 170	cca Pro	gga Gly	ccg Pro	gag Glu	cac His 175	aca Thr	528
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aga Arg	aag Lys 210	gta Val	cag Gln	ttt Phe	gct Ala	cct Pro 215	gag Glu	aca Thr	ccc Pro	ggc Gly	ccc Pro 220	cag Gln	cca Pro	tca Ser	gct Ala	672
gaa Glu 225	acc Thr	aca Thr	cgc Arg	cac His	ttc Phe 230	ctc Leu	atg Met	tct Ser	gac Asp	cgg Arg 235	agg Arg	tcc Ser	ctg Leu	cac His	cta Leu 240	720
gag Glu	gct Ala	tcc Ser	ctg Leu	gac Asp 245	aaa Lys	gag Glu	ctg Leu	tac Tyr	tac Tyr 250	cat His	ggg Gly	gaa Glu	ccc Pro	ctc Leu 255	aat Asn	768
gtc Val	aac Asn	gtc Val	cac His 260	gtc Val	acc Thr	aac Asn	aat Asn 265	tct Ser	gcc Ala	aag Lys	acc Thr	gtc Val	aag Lys 270	aag Lys	atc Ile	816
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cag Gln 290	tac Tyr	aag Lys	tgt Cys	cct Pro	gtg Val	gct Ala 295	cag Gln	ctt Leu	gaa Glu	caa Gln	gat Asp 300	gac Asp	cag Gln	gtg Val	tct Ser	912
ccc Pro 305	agt Ser	tcc Ser	aca Thr	ttc Phe	tgc Cys 310	aag Lys	gtg Val	tac Tyr	acc Thr	ata Ile 315	acc Thr	ccg Pro	ctg Leu	ctc Leu	act Thr 320	960
gac Asp	aac Asn	cga Arg	gag Glu	aag Lys 325	cgt Arg	ggc Gly	ctt Leu	gcc Ala 330	ctt Leu	cat His	ggg Gly	caa Gln	ctc Leu	aac Asn 335	cac His	1008
gaa Glu	cac His	acc Thr	aac Asn 340	ctg Leu	gct Ala	tcc Ser	agc Ser	acc Thr 345	att Ile	gtg Val	aag Lys	gag Glu	gga Gly 350	gcc Ala	aac Asn	1056
gag Glu	gtc Val	ctg Leu 355	gga Gly	atc Ile	cta Leu	gta Val	tcc Ser 360	tac Tyr	agg Arg	gtc Val	aag Lys	gtg Val 365	aag Lys	ctg Leu	gtg Val	1104

gtg tct cca ggc ggg gat ctc tcc gtg gag cta cct ttc gtc cta atg	1152
Val Ser Pro Gly Gly Asp Leu Ser Val Glu Leu Pro Phe Val Leu Met	
370 375 380	
cac ccc aag ccc cac cac cac atc acc ctt ccc cca ccc cag tca gcc	1200
His Pro Lys Pro His His His Ile Thr Leu Pro Pro Pro Gln Ser Ala	
385 390 395 400	
ccc cgg gaa ata gac atc cct gtg gat acc aac ctc att gaa ttc gat	1248
Pro Arg Glu Ile Asp Ile Pro Val Asp Thr Asn Leu Ile Glu Phe Asp	
405 410 415	
acc aac tat gcc aca gac gac gac atc gtg ttt gag gac ttt gcg agg	1296
Thr Asn Tyr Ala Thr Asp Asp Asp Ile Val Phe Glu Asp Phe Ala Arg	
420 425 430	
ctt cgg ctg aag ggg atg aag gat gac gac tgt gat gac cag ttc tgc	1344
Leu Arg Leu Lys Gly Met Lys Asp Asp Asp Cys Asp Asp Gln Phe Cys	
435 440 445	
gtc gac cag atc ttc gtg aag act ctg act ggt aag acc atc acc ctc	1392
Val Asp Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu	
450 455 460	
gag gtg gag ccc agt gac acc atc gag aat gtc aag gca aag atc caa	1440
Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln	
465 470 475 480	
gat aag gaa ggc att cct cct gat cag cag agg ttg atc ttt gcc gga	1488
Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly	
485 490 495	
aga cag ctg gaa gat ggt cgt acc ctg tct gac tac aac atc cag aaa	1536
Arg Gln Leu Glu Asp Gly Arg Thr Leu Ser Asp Tyr Asn Ile Gln Lys	
500 505 510	
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Glu Ser Thr Leu His Leu Val Leu Arg Leu Arg Gly Gly	
515 520 525	

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Leu Tyr Lys Ser Gly Leu Arg Ser Arg Ala Gln Ala Ser Asn Ser Ala
20 25 30

Val Asp Gly Thr Thr Arg Thr Met Gly Glu Lys Pro Gly Thr Arg Val
35 40 45

Phe Lys Lys Ser Ser Pro Asn Cys Lys Leu Thr Val Tyr Leu Gly Lys
Page 12

50

55

60

Arg Asp Phe Val Asp His Leu Asp Lys Val Asp Pro Val Asp Gly Val
65 70 75 80

Val Leu Val Asp Pro Asp Tyr Leu Lys Asp Arg Lys Val Phe Val Thr
85 90 95

Leu Thr Cys Ala Phe Arg Tyr Gly Arg Glu Asp Leu Asp Val Leu Gly
100 105 110

Leu Ser Phe Arg Lys Asp Leu Phe Ile Ala Thr Tyr Gln Ala Phe Pro
115 120 125

Pro Met Pro Asn Pro Pro Arg Pro Pro Thr Arg Leu Gln Asp Arg Leu
130 135 140

Leu Lys Lys Leu Gly Gln His Ala His Pro Phe Phe Phe Thr Ile Pro
145 150 155 160

Gln Asn Leu Pro Cys Ser Val Thr Leu Gln Pro Gly Pro Glu His Thr
165 170 175

Ala Lys Ala Cys Gly Val Asp Phe Glu Ile Arg Ala Phe Cys Ala Lys
180 185 190

Ser Ile Glu Gln Lys Ser His Lys Arg Asn Ser Val Arg Leu Ile Ile
195 200 205

Arg Lys Val Gln Phe Ala Pro Glu Thr Pro Gly Pro Gln Pro Ser Ala
210 215 220

Glu Thr Thr Arg His Phe Leu Met Ser Asp Arg Arg Ser Leu His Leu
225 230 235 240

Glu Ala Ser Leu Asp Lys Glu Leu Tyr Tyr His Gly Glu Pro Leu Asn
245 250 255

Val Asn Val His Val Thr Asn Asn Ser Ala Lys Thr Val Lys Lys Ile
260 265 270

Arg Val Ser Val Arg Gln Tyr Ala Asp Ile Cys Leu Phe Ser Thr Ala
275 280 285

Gln Tyr Lys Cys Pro Val Ala Gln Leu Glu Gln Asp Asp Gln Val Ser
290 295 300

Pro Ser Ser Thr Phe Cys Lys Val Tyr Thr Ile Thr Pro Leu Leu Thr
Page 13

305 310 315 320
 Asp Asn Arg Glu Lys Arg Gly Leu Ala Leu His Gly Gln Leu Asn His
 325 330 335
 Glu His Thr Asn Leu Ala Ser Ser Thr Ile Val Lys Glu Gly Ala Asn
 340 345 350
 Glu Val Leu Gly Ile Leu Val Ser Tyr Arg Val Lys Val Lys Leu Val
 355 360 365
 Val Ser Pro Gly Gly Asp Leu Ser Val Glu Leu Pro Phe Val Leu Met
 370 375 380
 His Pro Lys Pro His His His Ile Thr Leu Pro Pro Pro Gln Ser Ala
 385 390 395 400
 Pro Arg Glu Ile Asp Ile Pro Val Asp Thr Asn Leu Ile Glu Phe Asp
 405 410 415
 Thr Asn Tyr Ala Thr Asp Asp Asp Ile Val Phe Glu Asp Phe Ala Arg
 420 425 430
 Leu Arg Leu Lys Gly Met Lys Asp Asp Asp Cys Asp Asp Gln Phe Cys
 435 440 445
 Val Asp Gln Ile Phe Val Lys Thr Leu Thr Gly Lys Thr Ile Thr Leu
 450 455 460
 Glu Val Glu Pro Ser Asp Thr Ile Glu Asn Val Lys Ala Lys Ile Gln
 465 470 475 480
 Asp Lys Glu Gly Ile Pro Pro Asp Gln Gln Arg Leu Ile Phe Ala Gly
 485 490 495
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Asn Pro Ile Val Tyr Ala Phe Arg Ile Gly Lys Phe Arg Val Thr Phe
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Asp Glu Asp Ile Pro Glu Glu Arg Pro Asp Asp
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Asn Pro Ile Ile Tyr Pro Glu Ser Ser Lys Glu Phe Lys Arg Ala Phe
 1 5 10 15

Val Arg Ile Leu Gly Glu Gly Cys Arg Gly Arg Gly Arg Arg Arg Arg
 20 25 30

Arg Arg Arg Arg Arg Leu Gly Gly Cys Ala Tyr Thr Tyr Arg Pro Trp
 35 40 45

Thr Arg Gly Gly Ser Leu Glu Arg Ser Gly Ser Arg Lys Asp Ser Leu
 50 55 60

Asp Asp Ser Gly Ser Cys Leu Ser Gly Ser Gln Leu Thr Leu Pro Ser
 65 70 75 80

Ala Ser Pro Ser Pro Gly Tyr Leu Gly Arg Gly Ala Pro Pro Pro Val
 85 90 95

Glu Leu Cys Ala Phe Pro Glu Trp Lys Ala Pro Gly Ala Leu Leu Ser
 100 105 110

Ile Pro Ala Pro Glu Pro Pro Gly Arg Arg Gly Arg His Asp Ser Gly
 115 120 125

Pro Leu Phe Thr Phe Lys Leu Leu Thr Glu Pro Glu Ser Pro Gly Thr
 130 135 140

Asp Gly Gly Ala Ser Asn Gly Gly Cys Glu Ala Ala Ala Asp Val Ala
 145 150 155 160

Asn Gly Gly Pro Gly Phe Lys Ser Met Asn Pro Leu Ala Pro Gly Gln
 165 170 175

Phe

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Lys Lys Ile Leu Cys Arg Gly Asp Arg Leu Cys Arg Ile Val
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1 5 10 15

Arg Arg Ile Leu Cys Arg Pro Trp Thr Gln Thr Ala Trp
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Asn Pro Val Ile Tyr Thr Val Phe Asn Gln Asp Phe Arg Pro Ser Phe
1 5 10 15

Lys His Ile Leu Phe Arg Arg Arg Arg Arg Gly Phe Arg Gln
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Asn Pro Ile Ile Tyr Cys Arg Ser Pro Asp Phe Arg Lys Ala Phe Gln
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Gly Leu Leu Cys Cys Ala Arg Arg Ala Ala Arg Arg Arg His Ala Thr
20 25 30

His Gly Asp Arg Pro Arg Ala Ser Gly Cys Leu Ala Arg Pro Gly Pro
35 40 45

Pro Pro Ser Pro Gly Ala Ala Ser Asp Asp Asp Asp Asp Asp Val Val
50 55 60

Gly Ala Thr Pro Pro Ala Arg Leu Leu Glu Pro Trp Ala Gly Cys Asn
65 70 75 80

Gly Gly Ala Ala Ala Asp Ser Asp Ser Ser Leu Asp Glu Pro Cys Arg
85 90 95

Pro Gly Phe Ala Ser Glu Ser Lys Val
100 105

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Asn Pro Leu Ile Tyr Cys Arg Ser Pro Asp Phe Arg Ile Ala Phe Gln
1 5 10 15

Glu Leu Leu Cys Leu Arg Arg Ser Ser Leu Lys Ala Tyr Gly Asn Gly
20 25 30

Tyr Ser Ser Asn Gly Asn Thr Gly Glu Gln Ser Gly Tyr His Val Glu
35 40 45

Gly Glu Lys Glu Asn Lys Leu Leu Cys Glu Asp Leu Pro Gly Thr Glu
50 55 60

Asp Phe Val Gly His Gln Gly Thr Val Pro Ser Asp Asn Ile Asp Ser
65 70 75 80

Gln Gly Arg Asn Cys Ser Thr Asn Asp Ser Leu Leu
85 90

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Asn Pro Ile Ile Tyr Ala Phe Asn Ala Asp Phe Arg Lys Ala Phe Ser
1 5 10 15

Thr Leu Leu Gly Cys Tyr Arg Leu Cys Pro Ala Thr Asn Asn Ala Ile
20 25 30

Glu Thr Val Ser Ile Asn Asn Asn Gly Ala Ala Met Phe Ser Ser His
Page 17

35 40 45
 His Glu Pro Arg Gly Ser Ile Ser Lys Glu Cys Asn Leu Val Tyr Leu
 50 55 60
 Ile Pro His Ala Val Gly Ser Ser Glu Asp Leu Lys Lys Glu Glu Ala
 65 70 75 80
 Ala Gly Ile Ala Arg Pro Leu Glu Lys Leu Ser Pro Ala Leu Ser Val
 85 90 95
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 Thr Gln Asn Gly Gln His Pro Thr
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Leu Lys Ile Leu His Cys
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Asn Pro Val Ile Tyr Thr Thr Phe Asn Ile Glu Phe Arg Lys Ala Phe
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Leu Lys Ile Leu Ser Cys
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Asn Pro Val Ile Tyr Thr Val Phe His Ala Glu Phe Arg Asn Val Phe
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Arg Lys Ala Leu Arg Ala Cys Cys
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Asn Pro Val Ile Tyr Ala Phe Asn Ala Asp Phe Gln Lys Val Phe Ala
1 5 10 15

Gln Leu Leu Gly Cys Ser His Phe Cys Ser Arg Thr Pro Val Glu Thr
20 25 30

Val Asn Ile Ser Asn Glu Leu Ile Ser Tyr Asn Gln Asp Ile Val Phe
35 40 45

His Lys Glu Ile Ala Ala Ala Tyr Ile His Met Met Pro Asn Ala Val
50 55 60

Thr Pro Gly Asn Arg Glu Val Asp Asn Asp Glu Glu Glu Gly Pro Phe
65 70 75 80

Asp Arg Met Phe Gln Ile Tyr Gln Thr Ser Pro Asp Gly Asp Pro Val
85 90 95

Ala Glu Ser Val Trp Glu Leu Asp Cys Glu Gly Glu Ile Ser Leu Asp
100 105 110

Lys Ile Thr Pro Phe Thr Pro Asn Gly Phe His
115 120

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Asn Pro Met Cys Tyr Ala Leu Cys Asn Lys Ala Phe Arg Asp Thr Phe
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Arg Leu Leu Leu Leu Cys Arg Trp Asp Lys Arg Arg Trp Arg Lys Ile
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Pro Lys Arg Pro Gly Ser Val His Arg Thr Pro Ser Arg Gln Cys
35 40 45

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Asn Pro Ala Cys Tyr Ala Leu Cys Asn Ala Thr Phe Lys Lys Thr Phe
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Lys His Leu His Met Cys His Tyr Lys Asn Ile Gly Ala Thr Arg
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Asn Pro Val Cys Tyr Ala Leu Cys Asn Lys Thr Phe Arg Thr Thr Phe
1 5 10 15

Met Leu Leu Leu Cys Gln Cys Asp Lys Lys Lys Arg Arg Lys Gln Gln
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Tyr Gln Gln Arg Gln Ser Val Ile Phe His Lys Arg Ala Pro Glu Gln
35 40 45

Ala Leu
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Asn Pro Ala Cys Tyr Ala Leu Cys Asn Ala Thr Phe Lys Lys Thr Phe
1 5 10 15

Arg His Leu Leu Leu Cys Gln Tyr Arg Asn Ile Gly Thr Ala Arg
20 25 30

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Asn Pro Ile Cys Tyr Ala Leu Cys Asn Arg Thr Phe Arg Lys Thr Phe
1 5 10 15

Lys Met Leu Leu Leu Cys Arg Trp Lys Lys Lys Lys Val Glu Glu Lys
20 25 30

Leu Tyr Trp Gln Gly Asn Ser Lys Leu Pro
35 40

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Asn Pro Val Ile Tyr Ala Tyr Phe Asn Lys Asp Phe Gln Asn Ala Phe
1 5 10 15

Lys Lys Ile Ile Lys Cys Lys Phe
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Asn Pro Ile Ile Tyr Thr Met Ser Asn Glu Asp Phe Lys Gln Ala Phe
1 5 10 15

His Lys Leu Ile Arg Phe Lys Cys Thr Ser
20 25

<210> 26
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<400> 26

Asn Pro Leu Leu Tyr Thr Ser Phe Asn Glu Asp Phe Lys Leu Ala Phe
1 5 10 15

Lys Lys Leu Ile Arg Cys Arg Glu
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Asn Pro Ile Ile Tyr Cys Leu Arg Asn Gln Glu Val Lys Arg Ala Leu
1 5 10 15

Cys Cys Ile Leu His Leu Tyr Gln His Gln Asp Pro Asp Pro Lys Lys
20 25 30

Gly Ser Arg Asn Val
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Asn Pro Leu Ile Tyr Thr Leu Arg Asn Met Glu Val Lys Gly Ala Leu
1 5 10 15

Arg Arg Leu Leu Gly Lys Gly Arg Glu Val Gly
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<400> 29

Asn Pro Leu Phe Tyr Gly Phe Leu Gly Lys Lys Phe Lys Arg Tyr Phe
1 5 10 15

Leu Gln Leu Leu Lys Tyr Ile Pro Pro Lys Ala Lys Ser His Ser Asn
20 25 30

Leu Ser Thr Lys Met Ser Thr Leu Ser Tyr Arg Pro Ser Asp Asn Val
35 40 45

Ser Ser Ser Thr Lys Lys Pro Ala Pro Cys Phe Glu Val Glu
50 55 60

<210> 30
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<213> Homo sapiens

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Asn Pro Phe Leu Tyr Cys Phe Val Gly Asn Arg Phe Gln Gln Lys Leu
1 5 10 15

Arg Ser Val Phe Arg Val Pro Ile Thr Trp Leu Gln Gly Lys Arg Glu
20 25 30

Ser Met Ser Cys Arg Lys Ser Ser Ser Leu Arg Glu Met Glu Thr Phe
35 40 45

Val Ser

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Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys Phe Arg His Gly Leu
1 5 10 15

Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser Lys Asp Ser Leu Pro
20 25 30

Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser Ser Gly His Thr Ser
35 40 45

Thr Thr Leu
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<210> 32
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Asn Pro Leu Ile Tyr Ala Phe Ala Gly Glu Lys Phe Arg Arg Tyr Leu
1 5 10 15

Tyr His Leu Tyr Gly Lys Cys Leu Ala Val Leu Cys Gly Arg Ser Val
20 25 30

His Val Asp Phe Ser Ser Ser Glu Ser Gln Arg Ser Arg His Gly Ser
35 40 45

Val Leu Ser Ser Asn Phe Thr Tyr His Thr Ser Asp Gly Asp Ala Leu
50 55 60

Leu Leu Leu
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Asn Pro Ile Leu Tyr Asn Leu Val Ser Ala Asn Phe Arg His Ile Phe
1 5 10 15

Leu Ala Thr Leu Ala Cys Leu Cys Pro Val Trp Arg Arg Arg Arg Lys
20 25 30

Arg Pro Ala Phe Ser Arg Lys Ala Asp Ser Val Ser Ser Asn His Thr
35 40 45

Leu Ser Ser Asn Ala Thr Arg Glu Thr Leu Tyr
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Asn Pro Ile Ile Tyr Cys Cys Leu Asn Asp Arg Phe Arg Leu Gly Phe
1 5 10 15

Lys His Ala Phe Arg Cys Cys Pro Phe Ile Ser Ala Gly Asp Tyr Glu
20 25 30

Gly Leu Glu Met Lys Ser Thr Arg Tyr Leu Gln Thr Gln Gly Ser Val
35 40 45

Tyr Lys Val Ser Arg Leu Glu Thr Thr Ile Ser Thr Val Val Gly Ala
50 55 60

His Glu Glu Glu Pro Glu Asp Gly Pro Lys Ala Thr Pro Ser Ser Leu
65 70 75 80

Asp Leu Thr Ser Asn Cys Ser Ser Arg Ser Asp Ser Lys Thr Met Thr
85 90 95

Glu Ser Phe Ser Phe Ser Ser Asn Val Leu Ser
100 105

<210> 35
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Asn Pro Trp Ile Tyr Ala Ser Phe Ser Ser Ser Val Ser Ser Glu Leu
1 5 10 15

Arg Ser Leu Leu Cys Cys Ala Arg Gly Arg Thr Pro Pro Ser Leu Gly
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Pro Gln Asp Glu Ser Cys Thr Thr Ala Ser Ser Ser Leu Ala Lys Asp
35 40 45

Thr Ser Ser
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Asn Pro Val Ile Tyr Asn Leu Met Ser Gln Lys Phe Arg Ala Ala Phe
1 5 10 15

Arg Lys Leu Cys Asn Cys Lys Gln Lys Pro Thr Glu Lys Pro Ala Asn
20 25 30

Tyr Ser Val Ala Leu Asn Tyr Ser Val Ile Lys Glu Ser Asp His Phe
35 40 45

Ser Thr Glu Leu Asp Asp Ile Thr Val Thr Asp Thr Tyr Leu Ser Ala
50 55 60

Thr Lys Val Ser Phe Asp Asp Thr Cys Leu Ala Ser Glu Val Ser Phe
65 70 75 80

Ser Gln Ser

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<400> 37

Asn Pro Trp Ile Tyr Met Leu Phe Thr Gly His Leu Phe His Glu Leu
1 5 10 15

Val Gln Arg Phe Leu Cys Cys Ser Ala Ser Tyr Leu Lys Gly Arg Arg
20 25 30

Leu Gly Glu Thr Ser Ala Ser Lys Lys Ser Asn Ser Ser Ser Phe Val
35 40 45

Leu Ser His Arg Ser Ser Ser Gly Arg Ser Cys Ser Gln Pro Ser Thr
50 55 60

Ala
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Asn Pro Val Leu Tyr Ser Leu Met Ser Ser Arg Phe Glu Thr Phe Gln
 1 5 10 15

Glu Ala Leu Cys Leu Gly Ala Cys Cys His Arg Leu Arg Pro Arg His
 20 25 30

Ser Ser His Ser Leu Ser Arg Met Thr Thr Gly Ser Thr Leu Cys Asp
 35 40 45

Val Gly Ser Leu Gly Ser Trp Val His Pro Leu Ala Gly Asn Asp Gly
 50 55 60

Pro Glu Ala Gln Gln Glu Thr Asp Pro Ser
 65 70

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Asn Pro Leu Val Tyr Cys Phe Met His Arg Arg Phe Arg Gln Ala Cys
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Leu Glu Thr Cys Ala Arg Cys Cys Pro Arg Pro Pro Arg Ala Arg Pro
 20 25 30

Arg Ala Leu Pro Asp Glu Asp Pro Pro Thr Pro Ser Ile Ala Ser Leu
 35 40 45

Ser Arg Leu Ser Tyr Thr Thr Ile Ser Thr Leu Gly Pro Gly
 50 55 60

<210> 40
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Asn Pro Leu Val Tyr Ala Leu Ala Ser Arg His Phe Arg Ala Arg Phe
 1 5 10 15

Arg Arg Leu Trp Pro Cys Gly Arg Arg Arg Arg His Arg Ala Arg Arg
 20 25 30

Ala Leu Arg Arg Val Arg Pro Ala Ser Ser Gly Pro Pro Gly Cys Pro
35 40 45

Gly Asp Ala Arg Pro Ser Gly Arg Leu Leu Ala Gly Gly Gly Gln Gly
50 55 60

Pro Glu Pro Arg Glu Gly Pro Val His Gly Gly Glu Ala Ala Arg Gly
65 70 75 80

Pro Glu

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Asn Pro Ile Ile Tyr Thr Leu Thr Asn Lys Glu Met Arg Arg Ala Phe
1 5 10 15

Ile Arg Ile Met Ser Cys Cys Lys Cys Pro Ser Gly Asp Ser Ala Gly
20 25 30

Lys Phe Lys Arg Pro Ile Ile Ala Gly Met Glu Phe Ser Arg Ser Lys
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Ser Asp Asn Ser Ser His Pro Gln Lys Asp Glu Gly Asp Asn Pro Glu
50 55 60

Thr Ile Met Ser Ser Gly Asn Val Asn Ser Ser Ser
65 70 75

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Asn Pro Ile Ile Tyr Ala Leu Arg Ser Lys Asp Leu Arg His Ala Phe
1 5 10 15

Arg Ser Met Phe Pro Ser Cys Glu Gly Thr Ala Gln Pro Leu Asp Asn
20 25 30

Ser Met Gly Asp Ser Asp Cys Leu His Lys His Ala Asn Asn Ala Ala
35 40 45

Ser Val His Arg Ala Ala Glu Ser Cys Ile Lys Ser Thr Val Lys Ile
Page 27

50

55

60

Ala Lys Val Thr Met Ser Val Ser Thr Asp Thr Ser Ala Glu Ala Leu
 65 70 75 80

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Asn Pro Val Leu Tyr Ala Phe Leu Asp Glu Asn Phe Lys Arg Cys Phe
 1 5 10 15

Arg Gly Leu Cys Arg Lys Pro Cys Gly Arg Pro Asp Pro Ser Ser Phe
 20 25 30

Ser Arg Pro Arg Glu Ala Thr Ala Arg Glu Arg Val Thr Ala Cys Thr
 35 40 45

Pro Ser Asp Gly Pro Gly Gly Gly Arg Ala Ala
 50 55

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Asp Pro Phe Val Tyr Tyr Phe Val Ser His Asp Phe Arg Asp His Ala
 1 5 10 15

Lys Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val Lys Gln Met Gln
 20 25 30

Val Ser Leu Thr Ser Lys Lys His Ser Arg Lys Ser Ser Ser Tyr Ser
 35 40 45

Ser Ser Ser Thr Thr Val Lys Thr Ser Tyr
 50 55

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Asn Gly Glu Val Gln Ala Glu Leu Arg Arg Lys Trp Arg Arg Trp His
 1 5 10 15

Leu Gln Gly Val Leu Gly Trp Ser Ser Lys Ser Gln His Pro Trp Gly
20 25 30

Gly Ser Asn Gly Ala Thr Cys Ser Thr Gln Val Ser Met Leu Thr Arg
35 40 45

Val Ser Pro Ser Ala Arg Arg Ser Ser Ser Phe Gln Ala Glu Val Ser
50 55 60

Leu Val
65